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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,666	12/08/2003	Leah Marie Gayo-Fung	10624-136-999	6368

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,666	GAYO-FUNG ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-39,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-39,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed **7/7/06** presents remarks and arguments to the office action mailed **3/7/06**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 1-33 and 40 are canceled.

Claims 34-39 and 41-42 are pending in this office action.

Claims 41-42 are newly submitted.

Abstract

The objection to the abstract is withdrawn.

Double Patenting

I. Claims 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 - 49 of U.S. Patent No. 6,436923 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other. Both sets of claims refer to the same compounds (see

patented claims 1-49) and using the compound (see claim 34 in the current application) modulating ER-β in a cell. The current application claims anticipate the copending application claims

Applicant's arguments, filed, with respect to the above rejection have been fully considered and are persuasive. The rejection has been withdrawn.

II. Claims 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,686,351 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other. Both sets of claims refer to the same compounds (see patented claims 1-17) and using the compound (see claim 34 in the current application) modulating ER-β in a cell. The current application claims anticipate the patented claims

Applicant's arguments, filed, with respect to the above rejection have been fully considered and are persuasive. The rejection has been withdrawn.

III. Claims 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,372,739 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other. Both sets of claims refer to the same compounds (see patented claims 1-20) and using the compound (see claim 34 in the current

application) modulating ER-β in a cell. The current application claims anticipate the patented claims

Applicant's arguments, filed, with respect to the above rejection have been fully considered and are persuasive. The rejection has been withdrawn.

IV. Claims 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-44 of U.S. Patent co-pending application No. 10/085995. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicant's arguments, filed, with respect to the above rejection have been fully considered and are persuasive. The rejection has been withdrawn.

V. Claims 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-78 of U.S. Patent No. 6291456. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicant's arguments, filed, with respect to the above rejection have been fully considered and are persuasive. The rejection has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-35 and 37-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for breast and osteosarcoma cancer cells, does not reasonably provide enablement for bladder, uterus, ovary epiudidymis, kidney etc wherein the cell preferentially expresses ER-β over ER-α. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

Nature of the invention state of the prior art, relative skill of those in the art and the predictability of the art.

The nature of the invention is directed to a method of modulating an ER-β in a cell expressing ER-β, comprising contacting the cell with an effective amount of a compound having a structure as in claim 34. The claims as recited encompasese a wide variation of cells that expresses ER-β. For example Applicant is claiming the uterus cell as one such cell that expresses ER-β over ER-α. The reference Koehler et al. teach ER-β. Is a non-functional receptor in the adult uterus, teaching that ER-α is dominant in the uterus cell (see page 465, highlighted sec.) Also in the heart (cardiovascular) (see page 472) a controversial issue raises the question whether ER- exist in the heart muscle.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The amount of direction or guidance provided and the presence or absence of working examples

There are only two working examples with breast cells and osteosarcoma cells given in the specification. It is not shown from the breadth of claims that a wide representation of cells have over expressed ER-β over ER-α.

The quantity of experimentation necessary

Presently, guidance as to which particular disease have over expressed ER-β over ER-α in the claims is absent. In particular, with respect to methods of treating modulation of ER-β. As discussed in the reference Koehler et al. several experimentatiuon needs to be done for example with the heart where in it is not conclusive what ER- is expressed.

With regards to the use of the compounds.

Absent reasonable a priori expectations of success for using the various substituents of the compound, one skilled in the art would have to test extensively many disease states to see how modulation is carried out, since modulation is defined as The process, or result of the process, of varying a characteristic of a carrier in accordance with an information bearing signal.

Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise. The specification provided a number of ways that these compounds can be made but failed to show how series of these compounds can modulate the over expressed ER-β over ER-α.

Claims 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating breast and osteosarcoma cancers cells (bone), does not reasonably provide enablement for treating skin effects, mood swings, hot flashes, memory lost, hypercholesterolemia, hair loss, lung, colon, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at

1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The amount of direction or guidance provided and the presence or absence of working examples

There are only two working examples with breast cells and osteosarcoma cells given in the specification. Extrapolation of in-vitro to in vivo requires numerous trials. The specification does not show how the treatment of these numerous disease are treated with the claimed compound.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual treatment in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of treating every single disease in the instant claim 42.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of

administration, etc. and appropriate animal model and the determine when should preventing start with one of the claimed compounds and test the in the model system to determine whether or not the compound is effective for prevention of obesity in the said population type. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of muscle wasting disorder with any compound, one of skill in the art would have to then either envision a modification of the first pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new compound of the above, and test the system again.

Claims **37-38** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In particular, Applicant has not provided a description of the structure of a representative number of derivative compounds nor a description of the chemical and/or physical characteristics of a representative number of compounds nor a description of how to obtain a representative number of specific compounds.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in

possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

The ER-β in tissue expressing does not specify or give the possible tissues of ER-β.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
3/4/06

Ardin H. Marschel 2/14/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER